State of California—Health and Human Services Agency
Department of Health Services

California Department of Health Services

SANDRA SHEWRY
Director

ARNOLD SCHWARZENEGGER
Governor

March 1, 2006

Dear Chief Neonatalogist:

Subject: Changes to CAH Screening in the California Newborn Screening Program

With the addition of Congenital Adrenal Hyperplasia (CAH) to Californiaís Newborn Screening Program, neonatal intensive care units have had a disproportionate number of babies with positive newborn screening tests, requiring follow-up testing and evaluation. Most of those babies weigh less than 1000 grams and none has been subsequently found to have a diagnosis of CAH. This problem is not unique to California, but is experienced by all state newborn screening programs that test for CAH. The California NBS Program actually has one of the lowest false positive rates in the country at this time. However, we are taking steps to further decrease this rate by revising CAH screening protocols. This should result in a decrease, by approximately 70-80%, in the number of the babies less than 1000 grams with positive CAH screens. The changes in protocols were implemented on March 1, 2006.

Current protocol for <u>all babies</u>

All newborn screening (NBS) specimens are tested for CAH via measurement of 17-hydroxyprogesterone (17-OHP), utilizing an immunofluorescence assay (FIA). Currently, there are two classifications of positives, i.e., those with values over a specific cutoff that is considered high (designated as ìurgentî), and those that are borderline positive, i.e., above a lower cutoff but below the urgent cutoff, (deemed ìindeterminate positiveî). Cutoffs for both groups are weight-adjusted (see attached table of cutoffs by weight). Those tests in the urgent group are promptly reported out by phone to babiesí physicians/neonatologists for follow-up. Test values are in the ìindeterminate positive î range are not called out, but instead the specimens are sent from the regional newborn screening labs to the Genetic Disease Laboratory (GDL) to be tested by a different method (2nd tier testing) employing tandem mass spectrometry (MS/MS). MS/MS measures 17-OHP and the ratio of the sum of 17-OHP and androstenedione to cortisol. If the specimen is positive via these parameters, the babyís physician is then notified by phone. **Physicians need to be aware that the cutoff for 17-OHP utilizing MS/MS is different than the cutoff using FIA.**

New protocol for babies less than 1000 grams

- The cutoff designated as ìurgentî for babies less than 1000 grams is being raised from 250 nmol/L to 600 nmol/L. It is anticipated that babies less than 1000 grams with 17-OHP above 600 nmol/L will be very rare. As per the current protocol, these results will be called out to the babiesí physicians for follow-up.

- The ìindeterminate positive î range has changed from 220-250 nmol/L to 220-600nmol/L. This means that those babies whose values would have been in the urgent group requiring immediate follow-up, now will now have their specimens sent on for 2nd tier testing. Based upon our

experience since July 11, 2005, we predict that the vast majority of those tests will be deemed negative. 2nd Tier positives will be promptly reported to the babiesí physician/neonatologist for follow-up.

What hasnít changed

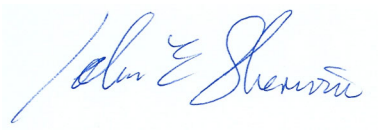
Staff members from the NBS Area Service Centers (ASC) call out positive screening results to physicians and provide assistance to them in referring these babies to CCS-approved endocrine centers/ physicians for diagnostic evaluation and testing. ASCs work closely with CCS to ensure that babies requiring follow-up are authorized to receive diagnostic services at a center, if necessary. For babies in NICUs, the Program recommends the collaboration of neonatologists and endocrinologists in the follow-up of positive tests. NBS coordinators track the babies with positive results until disease is diagnosed or ruled out. They will continue to request outcome information from you.

We are well aware of the time and effort that has been expended by neonatologists and NICU staff since the NBS Programís expansion last summer and are truly grateful for your support of the Program. We are hopeful that this protocol revision will assist all involved in the care of low birth weight babies and promote renewed confidence in newborn screening results for CAH. The feedback given to us by the neonatologists and NICU staffs has been invaluable in our evaluation of screening and of specific considerations in the NICU population with regard to CAH.

We have enclosed for your information a summary of the experience of the expanded screening up to this point. Please contact the ASC to which your facility is assigned (see attached list) if you have questions or comments about the changes described. As always, we appreciate feedback.

Thank you again for your past and continued support.

Sincerely,



John Sherwin, PhD, Acting Chief
Genetic Disease Branch

Enclosures

cc: Kathleen Velazquez, MPH, Chief
Newborn Screening Section

Pediatric Endocrinologists
NBS Area Service Center Coordinators
Chief of Pediatrics
NICU Nurse Manager